

**REMARKS**

Claims 1-83 were pending in the instant application. Claims 64-66 and 69-83 are canceled without prejudice as directed to a non-elected invention. Claims 40-63 are withdrawn from consideration as drawn to a non-elected invention. Claims 40-63 (Group II) are related to claims 1-39 and 67-68 (Group I) as product and process of use. It is the Applicant's understanding that, once the pending product claims are found allowable, any non-elected process claims (Group II, claims 40-63) will be rejoined and examined if such process claims include all of the limitations of the elected product claims (MPEP §821.04).

Claims 2, 5-18, 20, 23-26, 28-32, 37-38 and 64-68 have been canceled without prejudice. Claims 1, 3-4, 19, 21-22, 27, 33-36 and 39 have been amended. New claims 84-108 have been added. Accordingly, claims 1, 3-4, 19, 21-22, 27, 33-36, 39 and 84-108 will be pending after entry of the instant amendment. Applicant reserves the right to prosecute the claims as originally filed in this or a continuing application.

Support for the claim amendments and new claims can be found throughout the claims and specification as originally filed. No new matter has been added. In particular, support for the claim amendments and new claims can be found in the specification at least as indicated in the table below.

<i>Claim number</i>	<i>Support</i>
Claim 1	Original claim 8; Example 10, page 83, lines 19-32; Figure 10C
Claims 3-4	Original claims 3-4
Claim 19	Example 16, pages 92-93, and in particular at page 93, lines 6-9; Figure 16
Claims 21-22	Original claim 21; Example 10, page 84, lines 1-18 and 29-30; Figure 10D
Claim 27	Example 15, page 91, lines 26 through page 92, line 7; Figure 15B-C
Claims 33-36	Page 22, lines 20-23
Claims 39	Original claim 39
Claims 84-85	Original claim 8; Example 10, page 83, lines 19-32; Figure 10C
Claim 86	Example 13, pages 87-89, and particularly at page 88, lines 27-29; Figure 13A-D
Claim 87	Example 13, pages 87-89, and particularly at page 88, line 31 through page 89, line 2; Figure 13A-D
Claims 88-90	Page 41, lines 14-18
Claims 91-93	Example 16, pages 92-93, and in particular at page 93, lines 6-9; Figure 16
Claim 94	Example 16, pages 92-93, and particularly at page 93, lines 10-13
Claims 95-100	Page 41, lines 14-18
Claim 101-102	Original claim 19; Example 16, page 93, lines 2-9
Claims 103-105	Example 13
Claim 106-108	Page 41, lines 14-18

### Claim Objections

The Examiner objects to claims 5-39 as “being in improper form because a multiple dependent claim should refer to other claims in the alternative only, such as and/or, and cannot depend from any other multiple dependent claim.” Accordingly, the Examiner has not further

treated claims 5-39 on the merits. Claims 5-18, 20, 23-26, 28-32 and 37-38 have been canceled. Claims 19, 21, 22 and 27, as currently amended, are independent claims. The remaining multiple dependent claims (claims 33-36 and 39) have been amended so as to be in proper form.

**Claim Rejections Under 35 USC § 102**

**Claims 1-4 and 33-37**

Claims 1-4 and 33-37 are rejected under 35 U.S.C. § 102(b) as lacking novelty in view of Agrawal *et al.* (WO 94/01550). The Examiner relies on Agrawal *et al.* for teaching “a dsRNA comprising a sense and antisense strand [that] is complementary to a viral or cellular gene (see page 9, lines 30-36),” and for teaching that the “ds RNA[is] between 10 and 40 nucleobases (see Figures 6 and 7).” The Examiner further relies on Agrawal *et al.* for teaching a “dsRNA comprising nucleobases modifications for increased stability (see page 16, lines 24-36).”

Applicants respectfully traverse this rejection. The cited reference fails to teach each and every element of the present invention as recited in the claims amended herein.

Claims 2 and 37 have been canceled, thereby rendering the rejection moot as it pertains to these claims. Claims 34-36, as currently amended, no longer depend from any one of claims 1-4, thereby rendering the rejection moot as it pertains to these claims. Claim 1, as currently amended, is directed to a small interfering RNA (siRNA), comprising a sense strand and an antisense strand, wherein the antisense strand is complementary to the sense strand and has a sequence sufficiently complementary to a target mRNA sequence to direct target-specific RNA interference (RNAi), and wherein the antisense strand is modified by the substitution of ***each uridine with a 2'-fluoro uridine and each cytidine with a 2'-fluoro cytidine***, such that *in vivo* stability is enhanced as compared to a corresponding unmodified siRNA. Claims 3, 4 and 33, as currently amended, depend from claim 1, as well as from other claims.

Applicants submit that the amendment to claim 1 obviates the rejection to this claim as being anticipated by Agrawal *et al.*. In view of the foregoing, Applicants respectfully request

that the rejection of claims 1-4 and 33-37 under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

Claims 1-2 and 67-68

Claims 1-2 and 67-68 are rejected under 35 U.S.C. § 102(b) as lacking novelty in view of Parrish *et al.* (2000 *Molecular Cell*). The Examiner relies on Parrish *et al.* for teaching “a siRNA comprising a sense strand and an antisense strand wherein a modified nucleobases increases stability (see Figure 5) and wherein the antisense strand has a sequence sufficiently complementary to the target mRNA (see Figure 3).” The Examiner further relies on Parrish *et al.* for teaching a siRNA comprising a 2'-fluoro modified nucleotide on the antisense strand wherein the antisense strand is capable of adopting an A-form helix (see Figure 5). The Examiner states that Applicants disclose in the instant specification that “a siRNA comprising a 2' fluoro modified nucleotide is preferred for adopting an A-form helix (see page 21, lines 15-22).” Applicants respectfully traverse this rejection. The cited reference fails to teach each and every element of the present invention as recited in the claims amended herein.

Claims 2 and 67-68 have been canceled, thereby rendering the rejection moot as it pertains to these claims. Claim 1, as currently amended, is directed to a small interfering RNA (siRNA), comprising a sense strand and an antisense strand, wherein the antisense strand is complementary to the sense strand and has a sequence sufficiently complementary to a target mRNA sequence to direct target-specific RNA interference (RNAi), and wherein the antisense strand is modified by the ***substitution of each uridine with a 2'-fluoro uridine and each cytidine with a 2'-fluoro cytidine***, such that *in vivo* stability is enhanced as compared to a corresponding unmodified siRNA.

Applicants submit that the amendment to claim 1 obviates the rejection to claim 1 as being anticipated by Parrish *et al.*. In view of the foregoing, Applicants respectfully request that the rejection of claims 1-2 and 67-68 under 35 § 102(b) be reconsidered and withdrawn.

In view of the above amendments and remarks, it is believed that this application is in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

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Respectfully submitted,

By

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